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PROCESS FOR PRODUCTION OF FORMYLCYCLOPROPANECARBOXYLIC ESTER

Technical Field

The present invention relates to a process for production of a formylcyclopropanecarboxylate compound.

Background Art

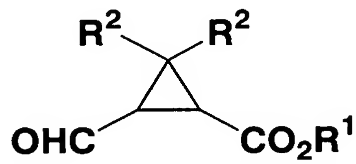
As a production method of methyl or ethyl 2,2-dimethyl-3-formylcyclopropanecarboxylate, there have been known a method of oxidizing methyl or ethyl 2,2-dimethyl-3-(hydroxymethyl)cyclopropanecarboxylate with pyridinium chlorochromate (Heterocycles, 23, 2859 (1985)), and a Swern oxidation reaction(Tetrahedron, 57, 6083 (2001)), etc. Since the oxidation with pyridinium chlorochromate has problems of waste-treatment due to the use of a heavy metal-containing reagent, and Swern oxidation has problems in that the control of the temperature was difficult due to large heat of the reaction and byproduction of the dimethyl sulfide which is a malodorous substance either of them have not always been satisfactory.

Disclosure of the Invention

According to the method of the present invention, a formylcyclopropanecarboxylate compound of formula (2) can be produced by oxidizing a cyclopropanecarboxylate compound of formula (2) with the advantage of avoiding the problem of waste-treatment or the temperature control and byproduction of the malodorous substance.

That is, the present invention provides a production

method of formylcyclopropanecarboxylate compound of formula (2):

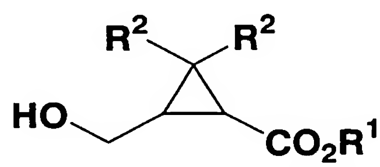


(2)

wherein R^1 and R^2 are as defined below,

which comprises reacting

a cyclopropanecarboxylate compound of formula (1):



(1)

wherein R^1 represent a linear, branched or cyclic alkyl group, a substituted or unsubstituted aryl group, or a substituted or unsubstituted aralkyl group,

R^2 represents a hydrogen atom or a methyl group,

with at least one oxidizer selected from the group consisting of hypochlorite, N-halosuccinimide, a trichloroisocyanuric acid and iodine,

in the presence of a nitroxy radical compound.

Best Mode for Carrying Out the Invention

In the cyclopropanecarboxylate compound of formula (1), hereinafter referred to as the cyclopropanecarboxylate compound (1), examples of the linear, branched or cyclic alkyl group represented by R^1 include, for example, a C1-15 linear, branched or cyclic alkyl group such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, n-hexyl, cyclohexyl, n-heptyl, n-octyl, n-nonyl, n-decyl,

menthyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, or the like.

Examples of the substituted or unsubstituted aryl group represented by R^1 include, for example, an unsubstituted aryl group such as phenyl, naphthyl or the like, and such a group as composed of these aryl groups in which one or two or more hydrogen atoms on the aromatic ring are replaced, for example, by a group selected from the alkyl group described above,

a halogen atom such as fluorine, chlorine, or the like,

an alkoxy group such as methoxy, ethoxy or the like,

an aryl group such as phenyl,

an aryloxy group such as phenoxy or the like, or

an alkoxycarbonyl group such as methoxycarbonyl or the like. Specific examples thereof include, for example, 4-methylphenyl group, 2,6-di(tert-butyl)-4-methylphenyl group, a 4-phenoxyphenyl group and the like.

Examples of the substituted or unsubstituted aralkyl group represented by R^1 include, for example, those groups composed of the alkyl group described above and the substituted or unsubstituted aryl group described above, and specific examples thereof include, for example, benzyl, 4-methoxybenzyl, 3-phenoxybenzyl, 2,3,5,6-tetrafluorobenzyl, 2,3,5,6-tetrafluoro-4-methylbenzyl, 2,3,5,6-tetrafluoro-4-methoxymethylbenzyl and the like.

Examples of the cyclopropanecarboxylate compound (1) include, for example,

methyl 2-(hydroxymethyl)cyclopropanecarboxylate,

ethyl 2-(hydroxymethyl)cyclopropanecarboxylate,

n-propyl 2-(hydroxymethyl)cyclopropanecarboxylate,

isopropyl 2-(hydroxymethyl)cyclopropanecarboxylate, n-butyl 2-(hydroxymethyl)cyclopropanecarboxylate, isobutyl 2-(hydroxymethyl)cyclopropanecarboxylate, sec-butyl 2-(hydroxymethyl)cyclopropanecarboxylate, tert-butyl 2-(hydroxymethyl)cyclopropanecarboxylate, n-pentyl 2-(hydroxymethyl)cyclopropanecarboxylate, n-hexyl 2-(hydroxymethyl)cyclopropanecarboxylate, cyclohexyl 2-(hydroxymethyl)cyclopropanecarboxylate, n-heptyl 2-(hydroxymethyl)cyclopropanecarboxylate, n-octyl 2-(hydroxymethyl)cyclopropanecarboxylate, n-decyl 2-(hydroxymethyl)cyclopropanecarboxylate, menthyl 2-(hydroxymethyl)cyclopropanecarboxylate, 2,6-di(tert-butyl)-4-methylphenyl 2-(hydroxymethyl)-cyclopropanecarboxylate, benzyl 2-(hydroxymethyl)cyclopropanecarboxylate, 4-methoxybenzyl 2-(hydroxymethyl)cyclopropanecarboxylate, 3-phenoxybenzyl 2-(hydroxymethyl)cyclopropanecarboxylate, 2,3,5,6-tetrafluoro-4-methoxymethylbenzyl 2-(hydroxyl-methyl)cyclopropanecarboxylate, methyl 3-(hydroxymethyl)-2,2-dimethylcyclopropane-carboxylate, ethyl 3-(hydroxymethyl)-2,2-dimethylcyclopropane-carboxylate, n-propyl 3-(hydroxymethyl)-2,2-dimethylcyclopropane-carboxylate, isopropyl 3-(hydroxymethyl)-2,2-dimethylcyclopropane-carboxylate, n-butyl 3-(hydroxymethyl)-2,2-dimethylcyclopropane-carboxylate,

isobutyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

sec-butyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

tert-butyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

n-pentyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

n-hexyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

cyclohexyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

n-heptyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

n-octyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

n-decyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

menthyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

2,6-di(tert-butyl)-4-methylphenyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

benzyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

4-methoxybenzyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

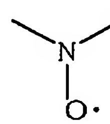
3-phenoxybenzyl 3-(hydroxymethyl)-2,2-dimethylcyclopropanecarboxylate,

2,3,5,6-tetrafluoro-4-methoxymethylbenzyl 3-(hydroxyl-

methyl)-2,2-dimethylcyclopropanecarboxylate, and the like.

These cyclopropanecarboxylate compound (1) have two isomers, which are a cis-isomer having the group shown by $-CO_2R^1$ and the group shown by $-CH_2OH$ on the same side with respect to the cyclopropane ring plane and a trans-isomer having the groups on the opposite side, and any one of the cis-isomer and the trans-isomer or a mixture thereof may be used in the present invention. In addition, the cyclopropanecarboxylate compound (1) has four optical isomers due to the presence of the two asymmetric carbon atoms and any one optical isomer thereof or a mixture of two or more of them may be used.

As the nitroxyl radical compound, a compound having the following structure represented by:



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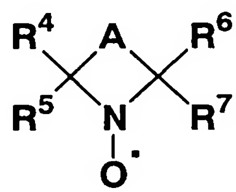
and having no hydrogen atom at the α-position to the nitrogen atom in the structure above may be used, and preferred is a nitroxy radical compound of formula (3):



(3)

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wherein R^4, R^5, R^6 and R^7 are the same or different and represent

a linear, branched or cyclic lower alkyl group, or

a linear, or branched lower alkenyl group,

an aryl group, an aralkyl group, or an acyl group, and

A represents a group represented by

$-CH_2COCH_2-$, $-COCH_2(CH_2)_n-$, or $-CHXCHY(CHZ)_n-$,

wherein n represents 0 or 1,

X, Y and Z are the same or different and represent a hydrogen atom, a hydroxyl group, a halogen atom, an amino group, an acylamino group, a carbamoyl group, a linear, branched or cyclic lower alkoxy group, a lower alkenyloxy group, an aryloxy group, an aralkyloxy group, or an acyloxy group.

Examples of the linear, branched or cyclic lower alkyl group include, for example, a C1-6 linear, branched or cyclic alkyl group such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, neopentyl, cyclopentyl, n-hexyl, cyclohexyl or the like.

Examples of the lower alkenyl group include, for example, a C2-6 linear, or branched alkenyl group such as vinyl, allyl, isopropenyl, 4-pentenyl, 5-hexenyl or the like.

Examples of the aryl group include, for example, a C6-10, aryl group such as phenyl, naphthyl or the like.

Examples of the aralkyl group include, for example, a C1-3 alkyl group substituted with the C6-C10 aryl group, and specific examples thereof include, for example, benzyl, phenylethyl, diphenylmethyl, phenylpropyl and the like.

Examples of the acyl group include, for example, a C1-6 aliphatic acyl group such as formyl, acetyl,propionyl, butyryl, valeryl, pivaloyl, hexanoyl or the like, or a C7-11 aromatic acyl group such as benzoyl or naphthoyl group or the like.

Examples of the halogen atom include, for example, a fluorine atom, a chlorine atom, a bromine atom, an iodine atom, and the like.

Examples of the acylamino group include, for example, an amino group substituted with the aliphatic or aromatic acyl group as described above such as acetylamino group, benzoylamino group or the like.

Examples of the linear, branched or cyclic alkoxy group include, for example, those composed of the lower alkyl groups as described above and an oxygen atom such as a C1-6 linear, branched or cyclic alkoxy group (e.g. methoxy, ethoxy, n-proxy, isoproxy, n-butoxy, sec-butoxy, tert-butoxy, n-pentyloxy, n-hexyloxy, cyclohexyloxy and the like).

Examples of the lower alkenyloxy group include, for example, those groups composed of the linear or branched lower alkenyl group described above and an oxygen atom such as a C2-6 linear or branched alkenyl group, (e.g. vinyloxy, 2-propenyloxy, 1-methylethenyloxy, 4-pentenyloxy, and 5-hexenyloxy and the like).

Examples of the aryloxy group include, for example, those composed of the aryl group as described above and an oxygen atom such as phenoxy, naphthoxy or the like.

Examples of the aralkyloxy group include, for example, those composed of the aralkyl group as described above and an oxygen atom such as a benzyloxy group, a phenethyloxy group or the like.

Examples of the acyloxy group include, for example, those composed of the acyl groups described above and an oxygen atom such as an acetoxy, propionyloxy, benzoyloxy or naphthoyloxy group or the like.

Examples of the nitroxy radical compound include, for example, 2,2,6,6-tetramethylpiperidine-1-oxyl,

4-acetoxy-2,2,6,6-tetramethylpiperidine-1-oxyl, 4-propionyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl, 4-benzoyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl, 4-methoxy-2,2,6,6-tetramethylpiperidine-1-oxyl, 4-ethoxy -2,2,6,6-tetramethylpiperidine-1-oxyl, 4-benzyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl, 4-acetamide-2,2,6,6-tetramethylpiperidine-1-oxyl, 4-oxo-2,2,6,6-tetramethylpiperidine-1-oxyl, 2,2,5,5-tetramethylpyrrolidine-1-oxyl and the like.

As the nitroxy radical compound a commercially available compound or a compound produced according to a similar manner disclosed in JP2002-145861A and the like may be used.

The nitroxy radical compound may be used as it is or after being dissolved or suspend in the solvent described below.

The amount of the nitroxy radical compound that may be used is not limited, and for example, an equivalent amount thereof is sufficient, and preferably, it may be a catalytic amount, which is less than the equivalent amount such as about 0.01 to 10 mol% to the cyclopropanecarboxylate compound (1).

At least one oxidizer selected from the group consisting of hypohalite, N-halosuccinimide, a trichloroisocyanuric acid, and iodine, hereinafter referred to as the oxidizer, is used for the present invention.

Examples of the hypohalite include, for example, an alkali metal or alkaline earth metal salt of hypohalogenic acid such sodium hypochlorite, potassium hypochlorite, calcium hypochlorite, and sodium hypobromite.

Examples of the N-halosuccinimide include, for example, N-chlorosuccinimide, N-bromosuccinimide, and the like.

The aqueous solution of the alkali metal hypohalite is preferred, more preferred is sodium hypochlorite.

The oxidizer may be used independently, or it may be used in combination as a mixture, moreover, it may be used as it is or it may be used, for example, in a form of an aqueous solution.

The oxidizer is usually used in the amount of about 1 to 5 moles, preferably about 1.5 to 4 moles per 1 mol of the cyclopropanecarboxylate compound (1).

The reaction of the invention is usually carried out by contacting or mixing the nitroxy radical, cyclopropanecarboxylate compound (1), and the oxidizer, and the mixing order is not particularly limited.

The reaction of the present invention is preferably conducted by keeping the pH of the reaction system at a range of from 6 to 13, more preferably at a range of from 6 to 10, still more preferably at a range of from 8 to 10. In order to control the pH of the reaction system, an acid such as a mineral acid or an organic acid, a base such as carbonate, bicarbonate, an alkali metal or alkaline earth metal hydroxide, or an alkali metal or alkaline earth metal carbonate, phosphate, hydrogenphosphate, an optional mixture of the acid, base, phosphate and hydrogenphosphate described above or a suitable buffer solution for maintaining the pH range described above is used.

Examples of the mineral acid include, for example, hydrochloric acid, sulfuric acid, phosphoric acid, boric acid, and the like.

Examples of the organic acid include, for example, acetic acid, propionic acid, benzoic acid, citric acid,

p-toluenesulfonic acid, etc.

Examples of the carbonate include, for example, alkali metal carbonate such as sodium carbonate, potassium carbonate, or the like.

Examples of the bicarbonate include, for example, alkali metal hydrogencarbonate such as sodium hydrogencarbonate, potassium hydrogencarbonate or the like.

Examples of the alkali metal hydroxide or the alkaline earth metal hydroxide include, for example, sodium hydroxide, potassium hydroxide, calcium hydroxide, and the like.

Examples of the alkaline earth metal carbonate include, for example, calcium carbonate and the like.

Examples of the phosphate include, for example, alkali metal phosphate such as sodium phosphate, potassium phosphate or the like, and alkali hydrogenphosphate such as potassium dihydrogenphosphate, dipotassium hydrogenphosphate, sodiumdihydrogenphosphate, disodium hydrogenphosphate or the like.

The acid, base, phosphate, hydrogenphosphate or mixtures thereof may be used as it is or may be used, for example, in a form of an aqueous solution. Preferably used is the bicarbonate, and more preferred is, for example, sodium hydrogencarbonate, also preferred is the hydrogenphosphate, and more preferred is, for example, alkali dihydrogenphosphate such as potassium dihydrogenphosphate, sodium dihydrogenphosphate or the like.

An effective amount of the acid, base, phosphate, hydrogenphosphate or mixtures thereof is used to maintain the pH of the aqueous phase of the reaction system within the

prescribed pH range, and can be added by selecting a suitable addition method such as an consecutive addition to the reaction system or addition as one portion at one time, and the reaction may be conducted using the same amount irrespective of the use of water solvent or the aqueous solution of them.

In the reaction of the present invention, about 0.1 to 10 moles of bicarbonate or dihydrogenphosphate are usually used per 1 mol of the compound of formula (1).

The reaction of the invention may be conducted in the absence of a solvent, for example, when the cyclopropanecarboxylate compound (1) is liquid, but it is usually conducted in the presence of a solvent. There is no limitation as to the solvent as long as it is inert to the reaction.

Examples of the solvent include, for example, aromatic hydrocarbon solvent such as toluene, xylene or mesitylene, halogenated hydrocarbon solvent such as dichloromethane, chloroform, carbontetrachloride, 1,2-dichloroethane or the like, an ether solvent such as diethyl ether, diisopropyl ether, or methyl tert-butyl ether or the like, a ketone solvent such as methyl isobutyl ketone, methyl tert-butyl ketone, or the like, water and mixtures of the solvents.

The amount of the solvent is not restricted. Moreover, when the reaction is conducted using a water-immiscible organic solvent and water, in a biphase a phase transfer catalyst may be also used in the reaction system.

Examples of the phase transfer catalyst include, for example, a quaternary ammonium halide such as tetra(n-butyl)ammonium bromide, tetra(n-butyl)ammonium

chloride, benzyltriethylammonium chloride, or tetraethylammonium chloride or the like.

The reaction temperature is usually -5ºC to 50ºC. After completion of the reaction, an organic phase containing the formylcyclopropanecarboxylate compound of formula (2), hereinafter referred to as formylcyclopropanecarboxylate compound (2), can be obtained, for example, by decomposing remaining oxidizer in the reaction solution with a reducing agent such as sodium thiosulfate, if necessary, and then adding water and/or a water-immiscible organic solvent to extract, and the organic phase is concentrated to isolate the formylcyclopropanecarboxylate compound (2). The isolated formylcyclopropanecarboxylate compound (2) may be further purified, if necessary, by conventionally employed purification process such as distillation, column chromatography or the like.

When an optically active compound is used as the cyclopropanecarboxylate compound (1), optically active formylcyclopropanecarboxylate compound (2) is obtained with the retention of configuration.

Examples of the thus obtained formylcyclopropanecarboxylate compound (2) include, for example,

methyl 2-formylcyclopropanecarboxylate,
ethyl 2-formylcyclopropanecarboxylate,
n-propyl 2-formylcyclopropanecarboxylate,
isopropyl 2-formylcyclopropanecarboxylate,
n-butyl 2-formylcyclopropanecarboxylate,
isobutyl 2-formylcyclopropanecarboxylate,

sec-butyl 2-formylcyclopropanecarboxylate,
tert-butyl 2-formylcyclopropanecarboxylate,
n-pentyl 2-formylcyclopropanecarboxylate,
n-hexyl 2-formylcyclopropanecarboxylate,
cyclohexyl 2-formylcyclopropanecarboxylate,
n-heptyl 2-formylcyclopropanecarboxylate,
n-octyl 2-formylcyclopropanecarboxylate,
n-decyl 2-formylcyclopropanecarboxylate,
menthyl 2-formylcyclopropanecarboxylate,
2,6-di(tert-butyl)-4-methylphenyl 2-formylcyclopropanecarboxylate,
benzyl 2-formylcyclopropanecarboxylate,
4-methoxybenzyl 2-formylcyclopropanecarboxylate,
3-phenoxybenzyl 2-formylcyclopropanecarboxylate,
2,3,5,6-tetrafluoro-4-methoxymethylbenzyl 2-formylcyclopropanecarboxylate,
methyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
ethyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
n-propyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
isopropyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
n-butyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
isobutyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
sec-butyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
tert-butyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
n-pentyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
n-hexyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
cyclohexyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
n-heptyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
n-octyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,

n-decyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
menthyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
2,6-di(tert-butyl)-4-methylpheny 2,2-dimethyl-3-formylcyclopropanecarboxylate,
benzyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
4-methoxybenzyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
3-phenoxybenzyl 2,2-dimethyl-3-formylcyclopropanecarboxylate,
2,3,5,6-tetrafluoro-4-methoxymethylbenzyl 2,2-dimethyl-3-formylcyclopropanecarboxylate and the like.

Example

The present invention is illustrated below in more detail with Examples, but it is not limited thereto. The analysis was conducted with gas chromatography, Internal standardization method

Example 1

To a 50 ml Schlenk tube were added 172 mg of ethyl 2,2-dimethyl-3-(hydroxymethyl)cyclopropanecarboxylate, 9.2 g of toluene, 0.18 g of water, 20 mg of dipotassium hydrogenphosphate, and 1.6 mg of 2,2,6,6-tetramethylpiperidine-1-oxyl, and then 931 mg of 12wt% aqueous sodium hypochlorite was added dropwise thereto under stirring at 20 ºC over 2 hrs. After completion of the addition, the reaction solution was maintained under stirring at that temperature for 30 minutes and then 1 ml of aqueous 5 wt% sodium thiosulfate was added thereto and stirred for 5 minutes. After

settled, phase separation gave an organic phase containing ethyl 2,2-dimethyl-3-formylcyclopropanecarboxylate.

Yield: 22%.

Example 2

To a 50 ml Schlenk tube were added 172 mg of ethyl 2,2-dimethyl-3-(hydroxymethyl)cyclopropanecarboxylate, 9.2g of toluene, 0.18 g of water, 20 mg of potassium dihydrogenphosphate, and 1.6 mg of 2,2,6,6-tetramethylpiperidine-1-oxyl, and then the temperature of the mixture was cooled to 0ºC under stirring. 931 mg of 12 wt% aqueous sodium hypochlorite was added dropwise thereto under stirring over 2 hrs. After completion of the addition, the reaction solution was maintained under stirring at that temperature for 30 minutes and then 1 ml of aqueous 5wt% sodium thiosulfate was added thereto and stirred for 5 minutes. After settled, phase separation gave an organic phase containing ethyl 2,2-dimethyl-3-formylcyclopropane-carboxylate.

Yield: 90%.

Example 3

The organic phase containing ethyl 2,2-dimethyl-3-formylcyclopropanecarboxylate was obtained in a similar manner as in Example 2 except that 13 mg of sodium hydrogencarbonate was employed in place of 20 mg of potassium dihydrogenphosphate employed in Example 2.

Yield: 89%.

Example 4

To a 50 ml Schlenk tube were added 791 mg of methyl 2,2-dimethyl-3-(hydroxymethyl)cyclopropanecarboxylate, 2.4 g of toluene, 0.80 g of water, 126 mg of sodium hydrogencarbonate, and 7.81 mg of 2,2,6,6-tetramethylpiperidine-1-oxyl, and 9.31 g of 12 wt% aqueous sodium hypochlorite was added dropwise thereto under stirring at 20 ºC over 1 hr. The pH was changed from 8.5 to 9.5. After completion of the addition, the reaction solution was maintained under stirring at that temperature for 30 minutes and then 5 ml of aqueous 5 wt% sodium thiosulfate was added thereto and stirred for 5 minutes. After settled, phase separation gave an organic phase containing methyl 2,2-dimethyl-3-formylcyclopropanecarboxylate.

Yield: 97%.

Example 5

The organic phase containing methyl 2,2-dimethyl-3-formylcyclopropanecarboxylate was obtained in a similar manner as in Example 4 except that 8.94 g of 12 wt% aqueous calcium hypochlorite was employed in place of 9.31 g of 12 wt% aqueous sodium hypochlorite employed in Example 4.

Yield: 29%.

Example 6

To a 50 ml Schlenk tube were added 791 mg of methyl 2,2-dimethyl-3-(hydroxymethyl)cyclopropanecarboxylate, 24.2 g of toluene, and 10.0 g of water, and then 420 mg of sodium hydrogencarbonate, 49.6 mg of calcium carbonate, 16.1 mg of tetrabutylammonium bromide, 7.81 mg of

2,2,6,6-tetramethylpiperidine-1-oxyl, and 1.34 g of N-chlorosuccinimide were added thereto under stirring at 20 ºC. After stirring for further 3 hrs at that temperature, 5 ml of aqueous 5wt% sodium thiosulfate was added thereto and stirred for 5 minutes. After settled, phase separation gave an organic phase containing methyl 2,2-dimethyl-3-formylcyclopropanecarboxylate.
Yield: 47%.

Example 7

To a 50 ml Schlenk tube were added 791 mg of methyl 2,2-dimethyl-3-(hydroxymethyl)cyclopropanecarboxylate, 2.4 g of toluene, 0.80 g of water, 126 mg of sodium hydrogencarbonate, and 7.81 mg of 2,2,6,6-tetramethylpiperidine-1-oxyl, and 1.16 g of trichloroisocyanurate was added thereto under stirring at 20 ºC. After stirring for further 2 hrs at that temperature, 5 ml of aqueous 5 wt% sodium thiosulfate was added thereto and stirred for 5 minutes. After settled, phase separation gave an organic phase containing methyl 2,2-dimethyl-3-formylcyclopropanecarboxylate.
Yield: 37%.

Example 8

To a 50 ml Schlenk tube were added 791 mg of methyl 2,2-dimethyl-3-(hydroxymethyl)cyclopropanecarboxylate, 24.2 g of toluene, 11.3 g of water, 1.26 g of sodium hydrogencarbonate, and 7.81 mg of 2,2,6,6-tetramethylpiperidine-1-oxyl, and 2.54 g of iodine was added thereto under stirring at 20 ºC. After stirring for further 3 hrs at that temperature, 5 ml of aqueous

5 wt% sodium thiosulfate was added thereto and stirred for 5 minutes. After settled, phase separation gave an organic phase containing methyl 2,2-dimethyl-3-formylcyclopropane-carboxylate.
Yield: 71%.

Example 9

To a 50 ml Schlenk tube were added 791 mg of methyl 2,2-dimethyl-3-(hydroxymethyl)cyclopropanecarboxylate, 24.2 g of toluene, 30.0 g of water, 15.4 mg of citric acid, 829 mg of disodium hydrogenphosphate and 7.81 mg of 2,2,6,6-tetramethylpiperidine-1-oxyl, and 9.31 g of 12 wt% aqueous sodium hypochlorite was added dropwise thereto under stirring at 20º over 1 hr. The pH of the aqueous phase changed from 8 to 10 during the reaction. After completion of the addition, the reaction solution was maintained under stirring at that temperature for 30 minutes and then 5 ml of aqueous 5wt% sodium thiosulfate was added thereto and stirred for 5 minutes. After settled, phase separation gave an organic phase containing methyl 2,2-dimethyl-3-formylcyclopropanecarboxylate.
Yield: 64%.

Example 10

The organic phase containing methyl 2,2-dimethyl-3-formylcyclopropanecarboxylate was obtained in a similar manner as in Example 9 except that 217 mg of citric acid and 534 mg of disodium dygrogenphosphate were used in place of 15.4 mg of citric acid and 829 mg of disodium

hygrogenphosphate. The pH of the aqueous phase of the reaction solution changed from 6 to 9 during the reaction.
Yield: 19%.

Example 11

The organic phase containing methyl 2,2-dimethyl-3-formylcyclopropanecarboxylate was obtained in a similar manner as in Example 9 except that 45.9 mg of sodium hydrogencarbonate and 43.7 mg of sodium hydroxide were used in place of 15.4 mg of citric acid and 829 mg of disodium hygrogenphosphate. The pH of aqueous phase of reaction solution changed from 10 to 11.
Yield: 12%.

Industrial Applicability

According to the method of the present invention, formylcyclopropanecarboxylate compound, which is a useful as synthetic intermediate for pyrethroid or furanone derivative can be produced with the advantage of avoiding a troublesome after-treatment after the reaction and byproduction of a malodorous substance (e.g. JP46-24695B, U.S. H No. 49, Tetrahedron, 57, 6083 (2001)).